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Restrictive impairment in patients with asthma ☆

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Summary
Background: Patients with asthma have intermittent or persistent airflow obstruction, most often manifested spirometrically by reduced forced expiratory volume in 1 s (FEV_1) and FEV_1/vital capacity (VC) ratio. In some patients, the VC may be reduced by air trapping, with an increase in functional residual capacity (FRC) and residual volume (RV) (pseudorestriction). We have reported 12 asthmatic patients with reduced VC and no increase in RV, i.e., a true restrictive impairment [Gill et al. True restrictive impairment in bronchial asthma. *Am J Respir Crit Care Med* 1999:**159**:A652].
Objectives: To confirm previous observations of true restrictive impairment (not attributable to air trapping) in patients with asthma, and to estimate its frequency in an asthmatic population.
Methods: Review of pulmonary function tests and clinical records of all post-pubertal patients diagnosed as asthma between January 2000 and September 2003 in a 184 bed inner city teaching hospital in Jamaica, Queens, New York. The clinical diagnosis of asthma was accepted when one or more of the following pulmonary function criteria were met: Positive bronchodilator response (BD), positive methacholine, repeated variability in spirometric values. Restriction was defined as decrease in total lung capacity (TLC) or decrease in VC with no increase in functional residual capacity (FRC) *plus* normal or high FEV_1/FVC ratio. Patients with any clinical finding consistent with restriction, including a decreased diffusing capacity (DL) or obesity (BMI >30) were excluded.
Results: A total of 100 of 413 (24%) patients with asthma had restriction; 21 of these met all exclusions (including DL and BMI) and 11 (of 46) patients with an increased BMI and normal DL normalized their FVC on BD therapy, demonstrating that their pre-BD restrictive impairment could not be attributed to obesity. Plethysmographic FRC was measured in 81 of the 100 patients with restriction and was increased in only seven.

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Conclusion: True restrictive impairment was noted in at least 32 of 413 asthmatics (8%), consistent with previous observations in asthma and reactive airways dysfunction syndrome. This finding is not widely recognized and should not preclude the diagnosis of asthma, BD testing or appropriate therapy for asthma.

Introduction

Asthma is a disorder characterized by increased reactivity of the airways. Patients with asthma have recurrent or persistent airflow obstruction, which is reversible either spontaneously or with appropriate therapy. An obstructive pattern is most often present, recognized by reduced forced expiratory volume in 1 s (FEV_1), and FEV_1 to forced vital capacity (FEV_1/FVC) or FEV_1/vital capacity (VC) ratio. Patients may have normal spirometry between attacks. In some patients, the FVC may be reduced due to air trapping, resulting in pseudo-restriction on spirometry in the presence of increased or normal total lung capacity (TLC), increased functional residual capacity (FRC) and increased residual volume (RV).

Several years ago, we reported on 12 asthmatics, observed in a 2 years interval at a medium-sized inner city teaching hospital, whose impairment on pulmonary function testing was restrictive[1]; those with any other reason for restriction, including many who were obese, were excluded. The diagnosis of asthma in these patients was often called into question because of the report of restrictive impairment and appropriate therapy cancelled or delayed. The nature of this series did not permit us to estimate the frequency of this finding in the asthmatic population. We therefore undertook a prospective review of pulmonary function in all asthmatic adults during a subsequent 45-month interval, to confirm the observation of restrictive impairment, to estimate its frequency and to consider its mechanisms.

Methods

Study design

We reviewed the pulmonary function tests (PFTs) and clinical and demographic features of all post-pubertal patients diagnosed as asthma between January 2000 and September 2003 at the St. Vincent Catholic Medical Center 184 bed Mary Immaculate Hospital (MIH) division, Jamaica, Queens, New York.

Methods and definitions

The PFTs were performed according to American Thoracic Society (ATS) specifications[2,3] using Sensomedics Vmax 22 for spirometry and diffusing capacity for carbon monoxide (DLCO) and model V for plethysmographic FRC; FRC was measured in all patients who could enter and tolerate the body box; fewer than 20% were unable to do so for orthopedic or psychologic reasons.

Forced exhalation time (FET) 100% $\geqslant$6 s or an expiratory plateau was required of all spirometric efforts accepted. Consistent with practice in the United States and with the predicted values, forced VC (FVC) was reported, although a separately performed slow VC was used to calculate lung volumes if it was larger than the FVC. Reference values for spirometric[4] and for static lung volumes[5] were race adjusted for people of African origin[2] and those for DLCO[6] were adjusted for smoking. The lower 95% confidence interval was used to define abnormality.

The diagnosis of asthma was accepted when the following criteria were met:

1. Physician diagnosis of asthma with intermittent or persistent symptoms of shortness of breath, wheezing and/or chest tightness.
2. Confirmation by one of the following pulmonary functional findings:
   (a) Repeated variability in well-performed spirometic values (increase in FEV_1 or FVC).
   (b) Positive bronchodilator (BD) responses (increase in FEV_1 or FVC $\geqslant$12% and 200 mL from baseline).
   (c) Positive methacholine challenge (20% fall in FEV_1 at a dose $\leqslant$8 μg/mL).

Restriction was defined as all of the following:

1. Decrease in TLC or decrease in VC with no increase in FRC. FRC was preferred to RV because it is directly measured, and because of the difficulty in measuring ERV especially in obese patients.
2. Normal or high FEV_1/FVC ratio.

Patients with another significant respiratory diagnosis, congestive heart failure, radiographic findings of interstitial lung disease (ILD), neuromuscular disorder or skeletal deformity were excluded. Those with decreased DL and/or BMI >30 were placed in separate categories.

Results

As seen in Table 1, of 413 patients with asthma, 107 (26%) had spirometric results within the normal range, 180 (44%) were obstructed (decreased FEV_1, decreased FEV_1/FVC, normal FVC) and an additional 26 (6%) showed spirometric mixed obstructive-restrictive impairment (decreased FEV_1, decreased FEV_1/FVC with decreased FVC). Of the 100 asthmatic patients (24% of the total) with spirometric restriction alone, plethysmographic FRC was measured in 81 and was increased in only seven. That FRC was not increased ruled out ''pseudorestriction'' secondary to air trapping. Of these 100 patients with restriction, 63 had a BMI >30 (including 17 who also had a decreased DL) and 16 had a decreased DL with a normal BMI. There were 21 patients with restriction who had both DL and BMI within the normal range.

Of the 46 patients with an increased BMI and normal DL, 11 normalized their FVC post-BD or within 4 weeks on treatment with no decrease in BMI. These 11 were added to the 21 with normal BMI and DL since their initial restrictive impairment could not be attributed to obesity.

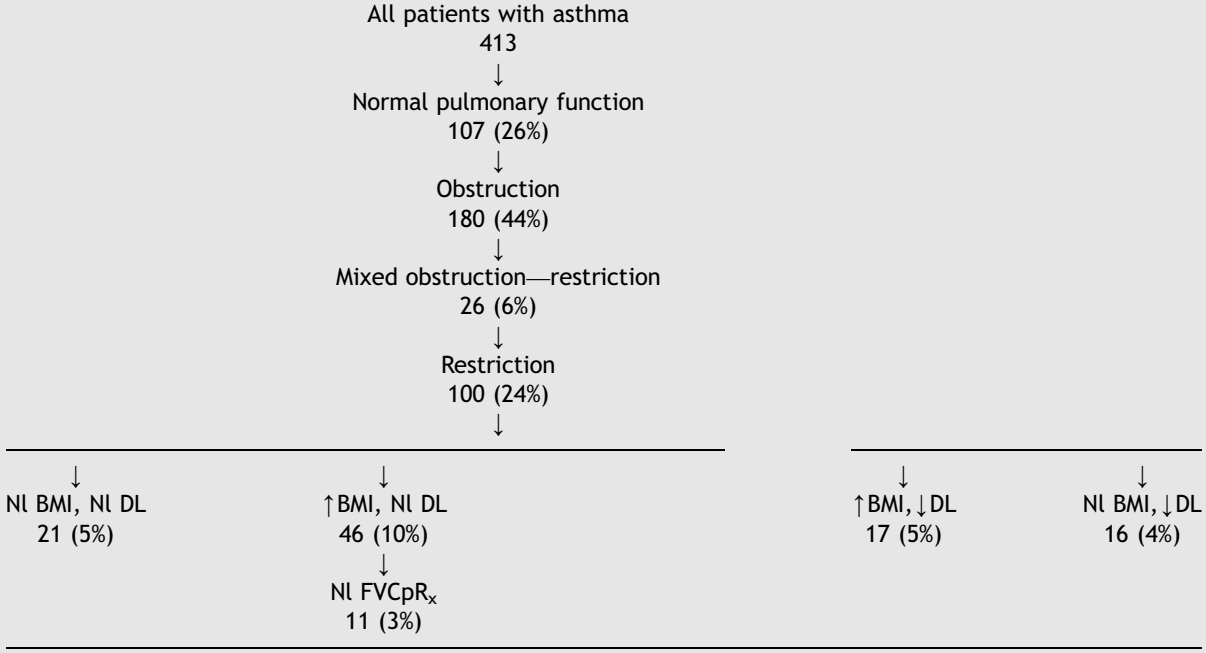
True restrictive impairment was thus noted in at least 32 of 413 asthmatics (8%). All 32 had normal DL and of the 25 measured, 22 (88%) had normal or decreased plethysmographic FRC. It is likely that restriction was similarly attributable to asthma in some of the 32 patients who had restriction and decreased DL with no clinical or radiographic evidence of ILD.

Age range of the 32 asthmatics with restrictive impairment and no other explanation was 21–64; 24 (75%) were female, 18 (56%) were never-smokers, 3 (9%) former smokers; and 11 (34%) current smokers. By ethnicity, 10 were Black, 8 Asian, 7 White, 6 Hispanic and one Amerindian.

Discussion

The findings in these 32 asthmatic patients with restriction mirror the 12 previously reported from this hospital[1] after the same process of exclusion in both series. We rigidly ruled out other conditions which could contribute to restrictive impairment. It is likely that in certain asthmatic patients with restrictive impairment who were excluded, their restrictive impairment was similarly caused or contributed to by their asthma.

Table 1 Distribution of pulmonary function impairments in 413 patients with asthma.



Restriction in asthma was reported in two patients by Colp and Williams,[7] and attributed to reversible closure of the airways. Hudgel and coworkers[8] reported a young woman with spontaneous and exercise-induced dyspnea. During a typical episode, lung volumes decreased markedly (TLC from 5.3 to 2.6 L, VC from 3.8 to 1.2 L), and FEV_1 fell from 3.0 to 1.0 L while FEV_1/FVC ratio increased (from 0.78 to 0.85) and specific airways conductance and flow rates measured at absolute lung volume increased. Static compliance decreased and elastic recoil increased. The authors attributed these changes to muscular contraction of small airways. Dawson cites closure of the airways in young patients with seemingly mild bronchospasm; FVC decreases and obstruction is not detected because flow may be preserved in other airways.[9]

One of the present authors (A.M.) reported restrictive impairment in 21 patients with asthma over a 4-year period in a part-time pulmonary practice[10]; patients with other causes for restriction were excluded, as in the present study. Full lung volumes were generally not available to rule out pseudorestriction.

True restrictive impairment with decreased FRC and TLC and positive BD response has been described in reactive airways dysfunction syndrome,[11] most recently as a result of exposure at Ground Zero following the terrorist attack on the World Trade Center. Of 599 non-smokers, 21% showed restriction on spirometry. Unfortunately, lung volumes were not measured.[12] All exposure categories sustained equivalent reductions in mean FVC and FEV_1 with little change in FEV_1/FVC ratio.[13]

One third of the patients (33 of 100) with restrictive impairment had a decreased DL with no clinical or radiographic evidence of pulmonary interstitial or vascular disease. We have noted a decreased DL in other patients with asthma and are preparing a report on this finding.

An unpublished survey of the asthma population of our hospital ($n = 238$) undertaken during the time of the earlier series showed 68% were females and 39% obese; 13% of the males and 51% of the females were obese. Pertinent to the present report, 33% of the obese patients showed restrictive impairment on spirometry, as did 15% of the non-obese. Unlike the present report, other possible causes for restriction were not systematically excluded. The patients with restrictive impairment in the present series reflect the gender and ethnic distributions of our asthma population but are even more likely to be obese (65%).

The high prevalence of obesity in asthma has been the subject of extensive investigation[14,15] and review.[16,17] In a 2000 Centers for Disease Control and Prevention survey of almost 200,000 adults in all 50 states, odds ratios for both lifetime and current asthma were increased in the obese (1.54 and 1.65, respectively), more so in women.[18]

Conclusion

True restrictive impairment was noted in at least 32 of 413 asthmatics (8%), consistent with previous observations in asthma and reactive airways dysfunction syndrome. This finding is not widely recognized and should not preclude the diagnosis of asthma, BD testing or appropriate therapy for asthma.

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